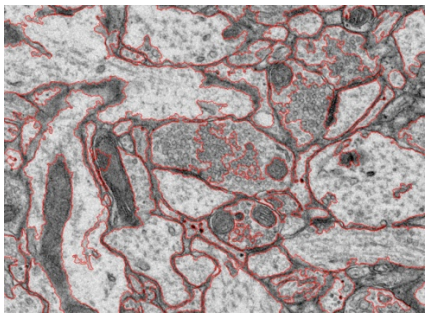
# Geometric Modeling and Visualization

## http://www.cs.utexas.edu/~bajaj/cs384R08/

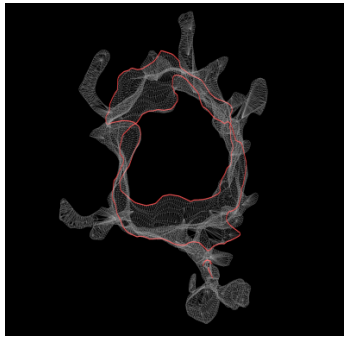
T, TH 9:30 – 10:45pm

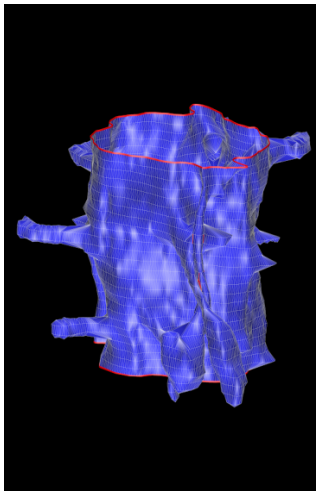
Taylor 3.144

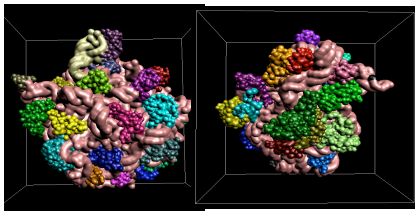
- Spatially realistic modeling to simulate and visually depict "How THINGS WORK" at multiple scales

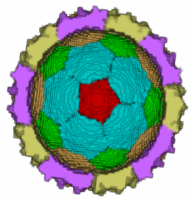


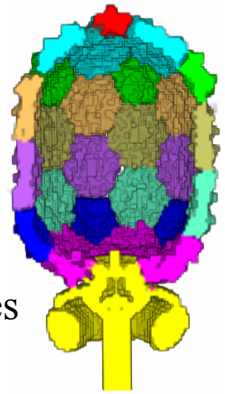
Neuronal Processes



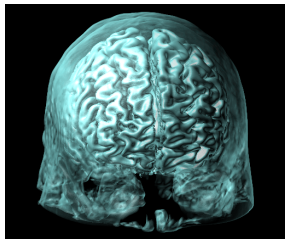


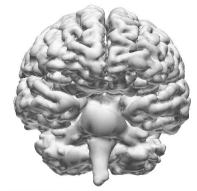


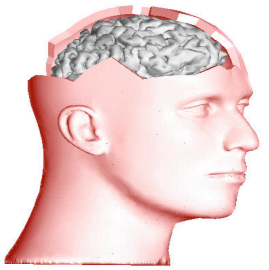




Ribosomes & Viruses







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# CS384R/CAM395T

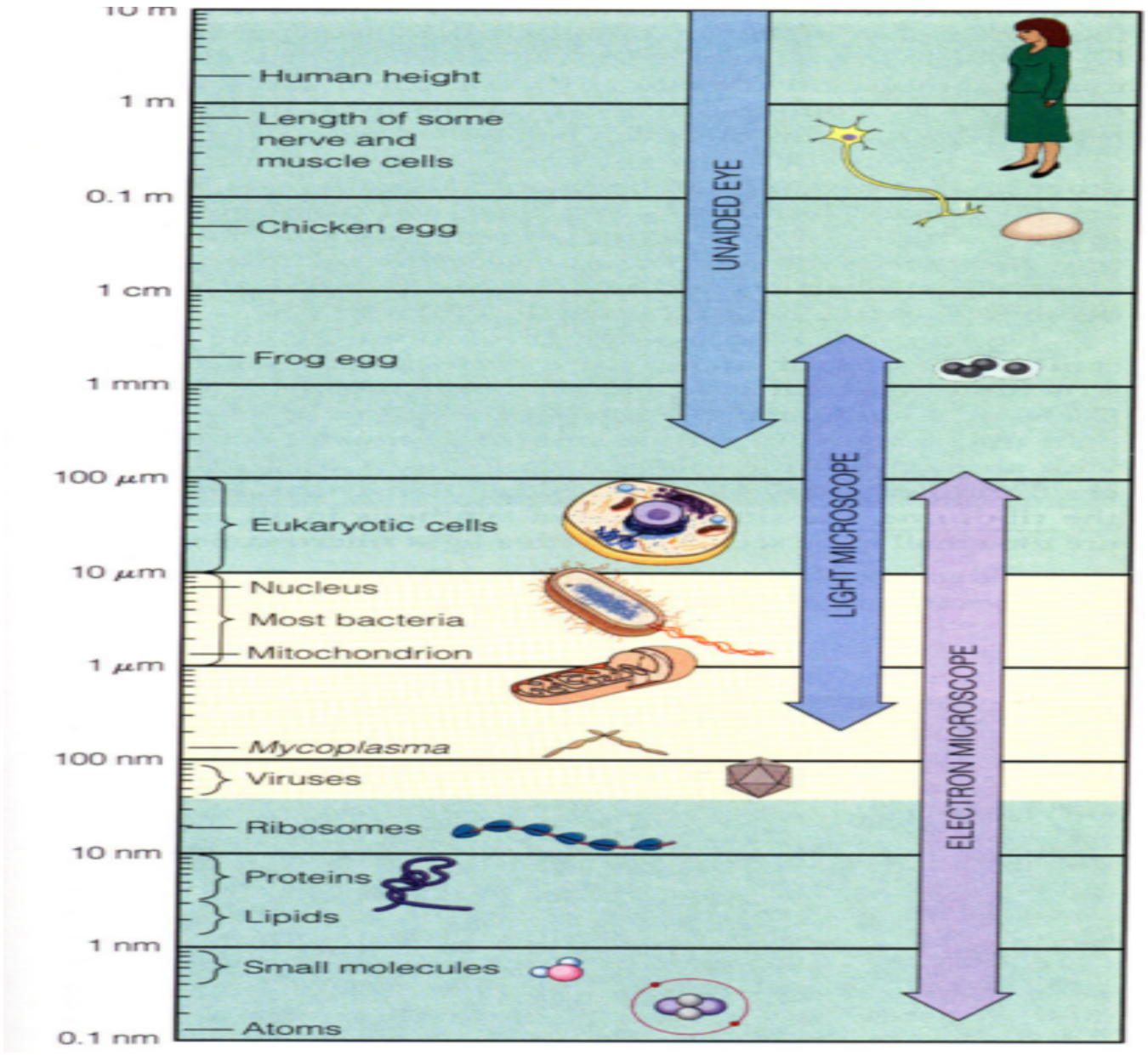
1. Imaging2Models: filtering, contrast enhancement, classification, symmetry detection, segmentation, skeletonization, subunit identification, matching, compression, reconstruction

2. Models2Analytics I: surfaces, finite element meshing, spline representations, feature identification, symmetry detection, shape segmentation, matching & complementary docking, flexibility, fluids

3. Models2Analytics II: polar and non-polar energetics, forces, torques, dynamics, cubature, discrete differential operators, sparsifiers, preconditioners

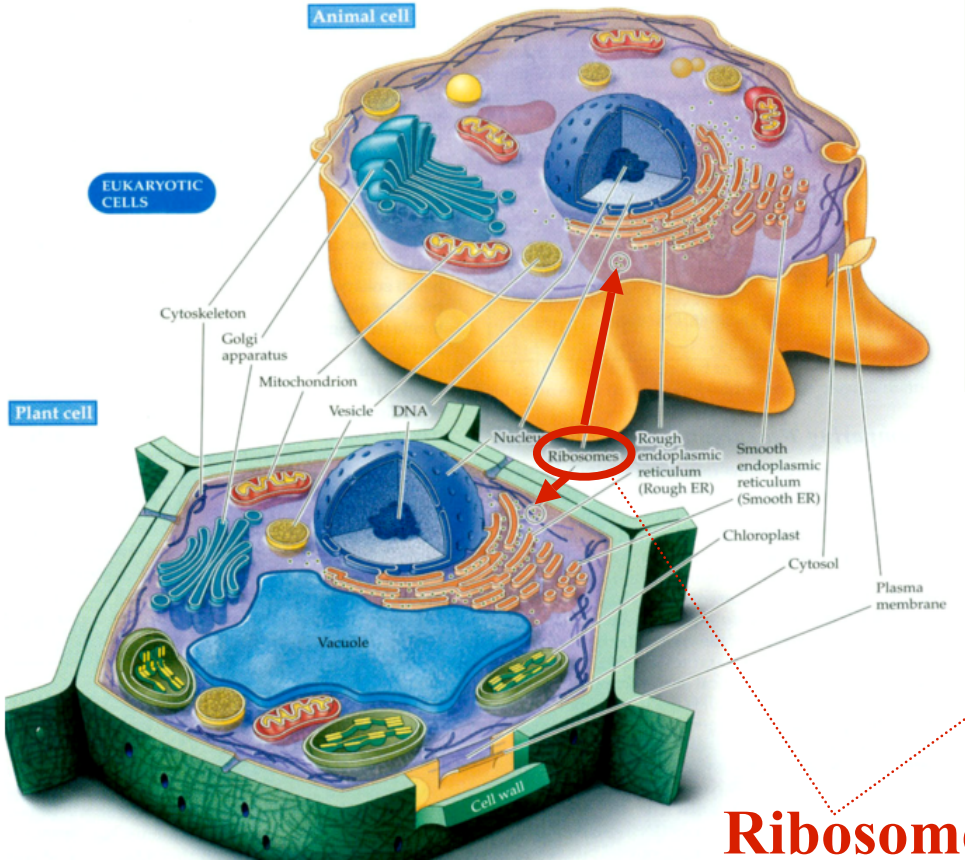
4. Analytics2Informatics I: differential/integral/ combinatorial properties, active sites, regions of interest, MACT analysis

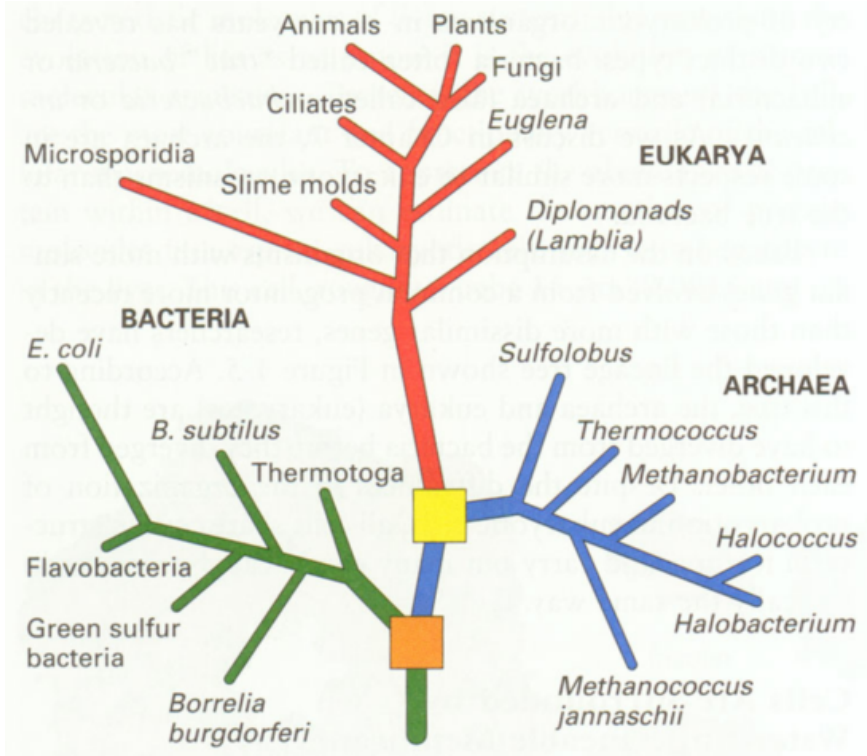
5. Analytics2Informatics II: multi-dimensional transfer functions, visible surface and volume rendering, function on surface, VisPortal


10 m
Human height
1 m
Length of some nerve and muscle cells
0.1 m
Chicken egg
1 cm
Frog egg
1 mm
100 μm
Eukaryotic cells
10 μm
Nucleus
Most bacteria
Mitochondrion
1 μm
Mycoplasma
100 nm
Viruses
Ribosomes
10 nm
Proteins
Lipids
1 nm
Small molecules
0.1 nm
Atoms
UNAIDED EYE
LIGHT MICROSCOPE
ELECTRON MICROSCOPE

# The Tree of Life?

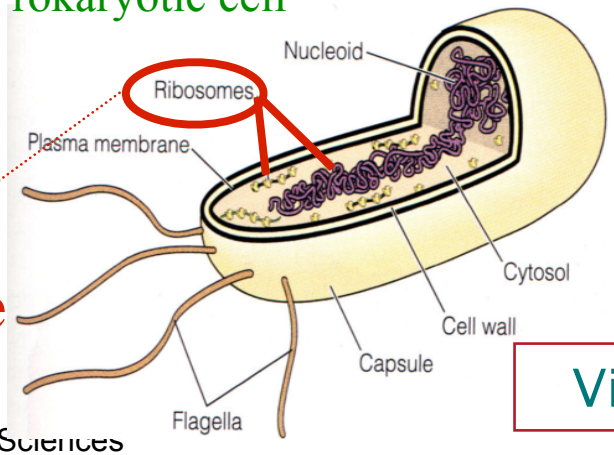
Eukaryotic cell




Archaebacteria cell

Prokaryotic cell




**Ribosome**

Viruses?

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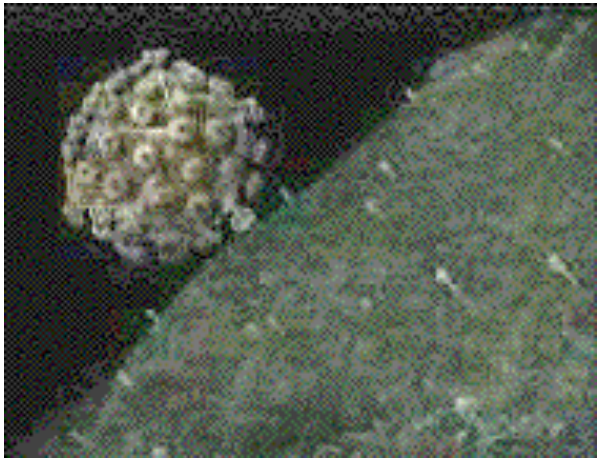
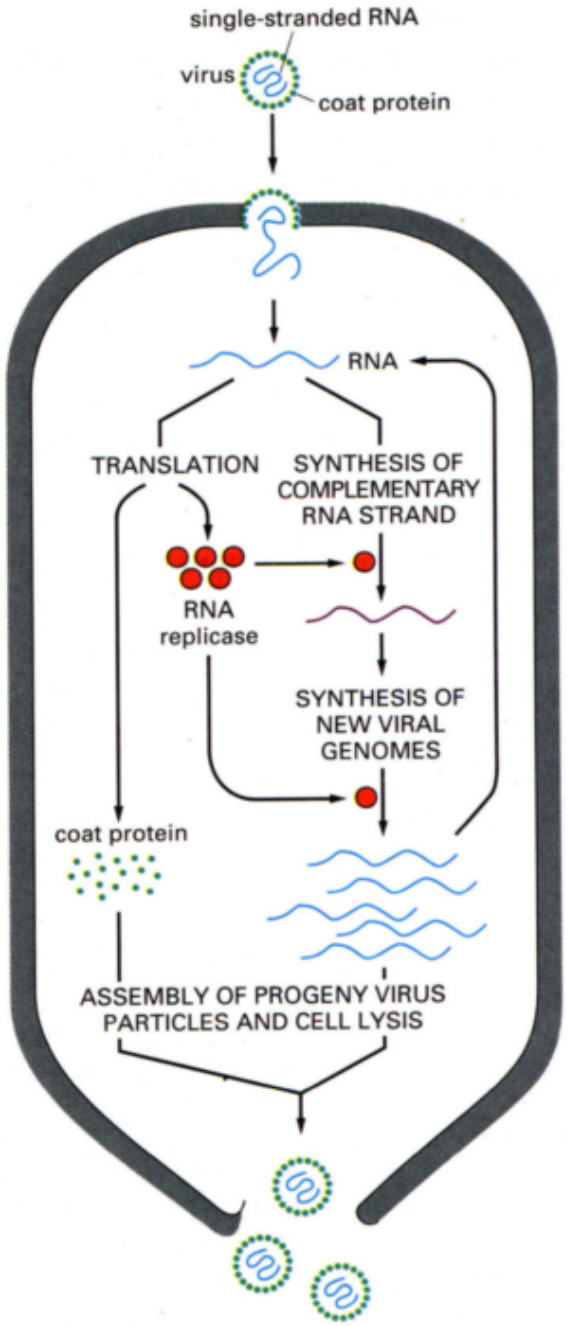
# The Life Cycle of Viruses





# Imaging2Models

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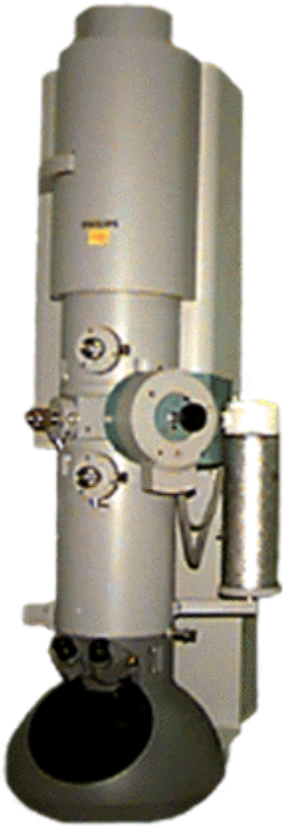
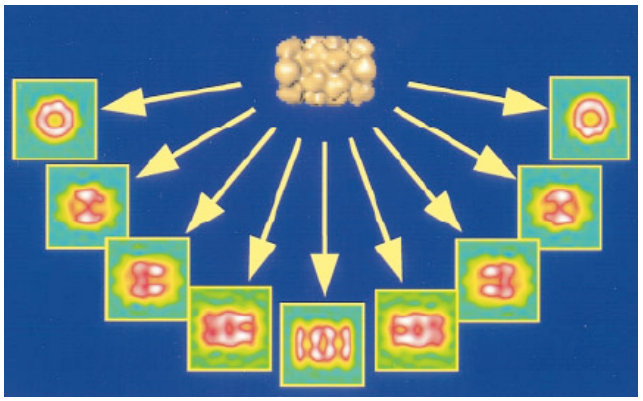
# Tools for 3D Structure Determination

- X-ray crystallography (diffraction)
  - Atomic resolution
  - Difficulties (experimental, computational)
- Nuclear magnetic resonance (NMR)
  - Atomic resolution
  - Limited to relatively small units
- Electron Microscope
  - Cryo-electron tomography
    - Low resolution (20Å – 200Å)
    - Good for whole cell or cell organelles
  - Single particle cryo-EM
    - Intermediate resolution (5Å – 20Å)
    - Computationally more complicated

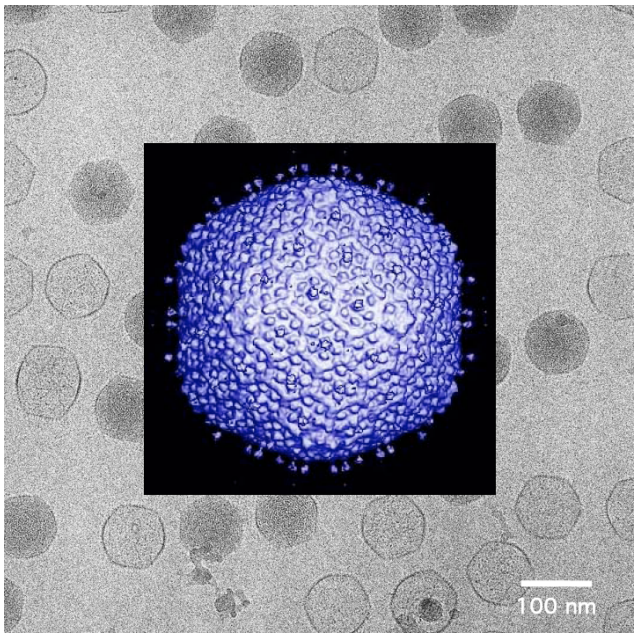


Picture from http://www.itg.uiuc.edu/ms/equipment/microscopes/tem/



Electron tomography

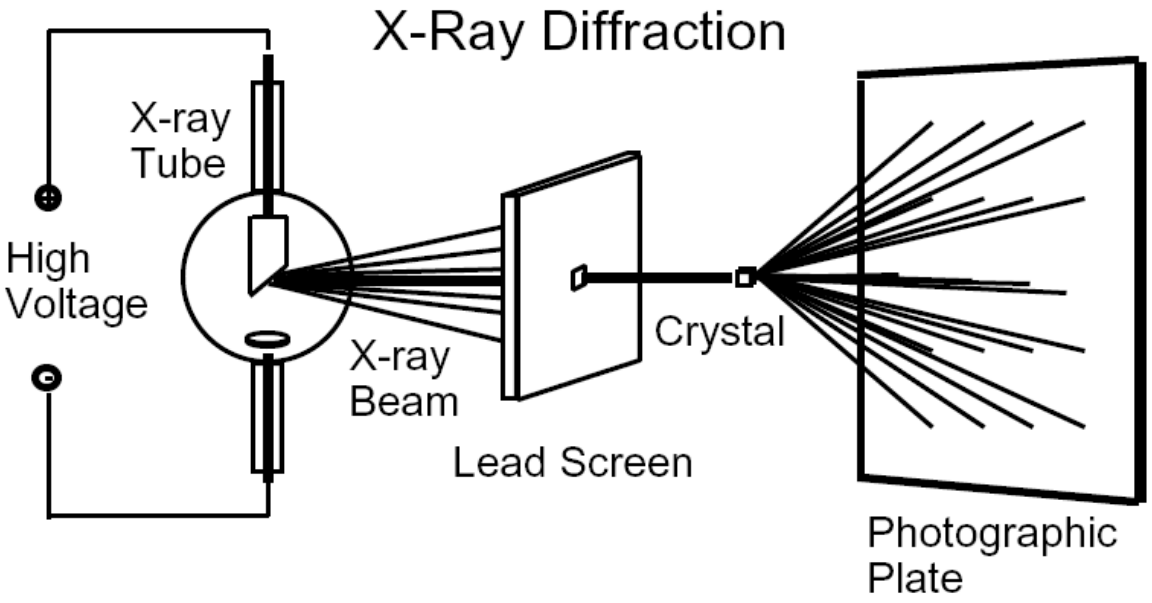
(Picture from A.J. Koster et al, JSB, 1997)

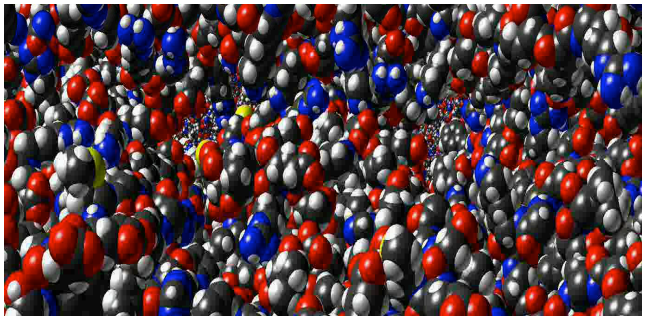



Single particle cryo-EM

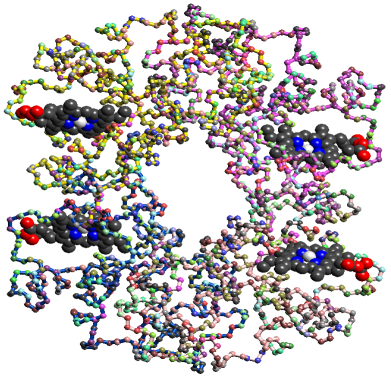
(Picture from Tim S. Baker)

# X-ray diffraction

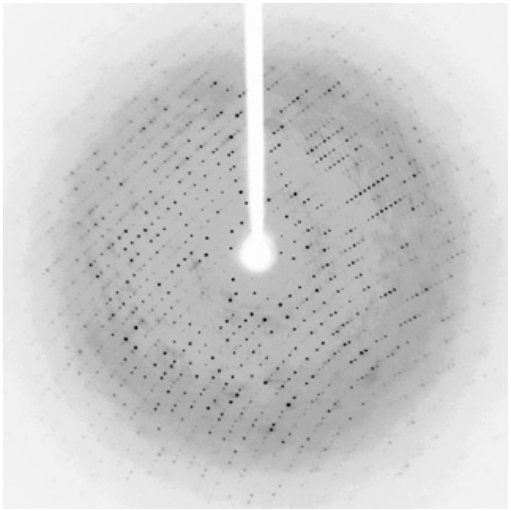


Microtubule

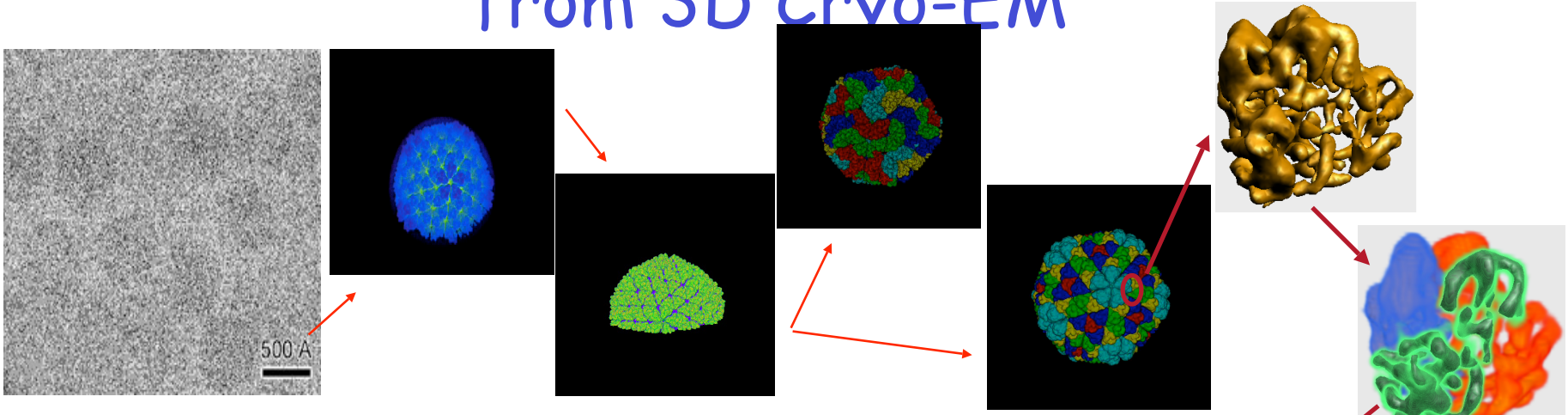


human deoxy-Hemoglobin



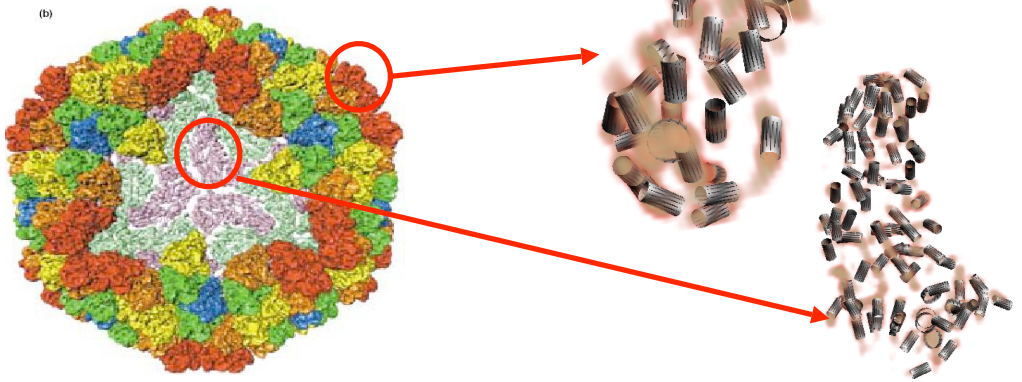
**Protein Data Bank**

# Sub-nanometer Structure Elucidation from 3D Cryo-EM




Cryo-EM →FFT based 3D Reconstruction
→Anisotropic and Vector Diffusion Filtering →
Structure Segmentation
→Quasi-Atomic Modeling
→Visualization

Rice Dwarf Virus



**Sponsored by NSF, NIH, NVH

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(Collaborators: Dr. Wah Chiu,NCMI, Baylor College of Medicine, Dr. A. Sali, UCSF, Dr. Tim Baker, UCSD)

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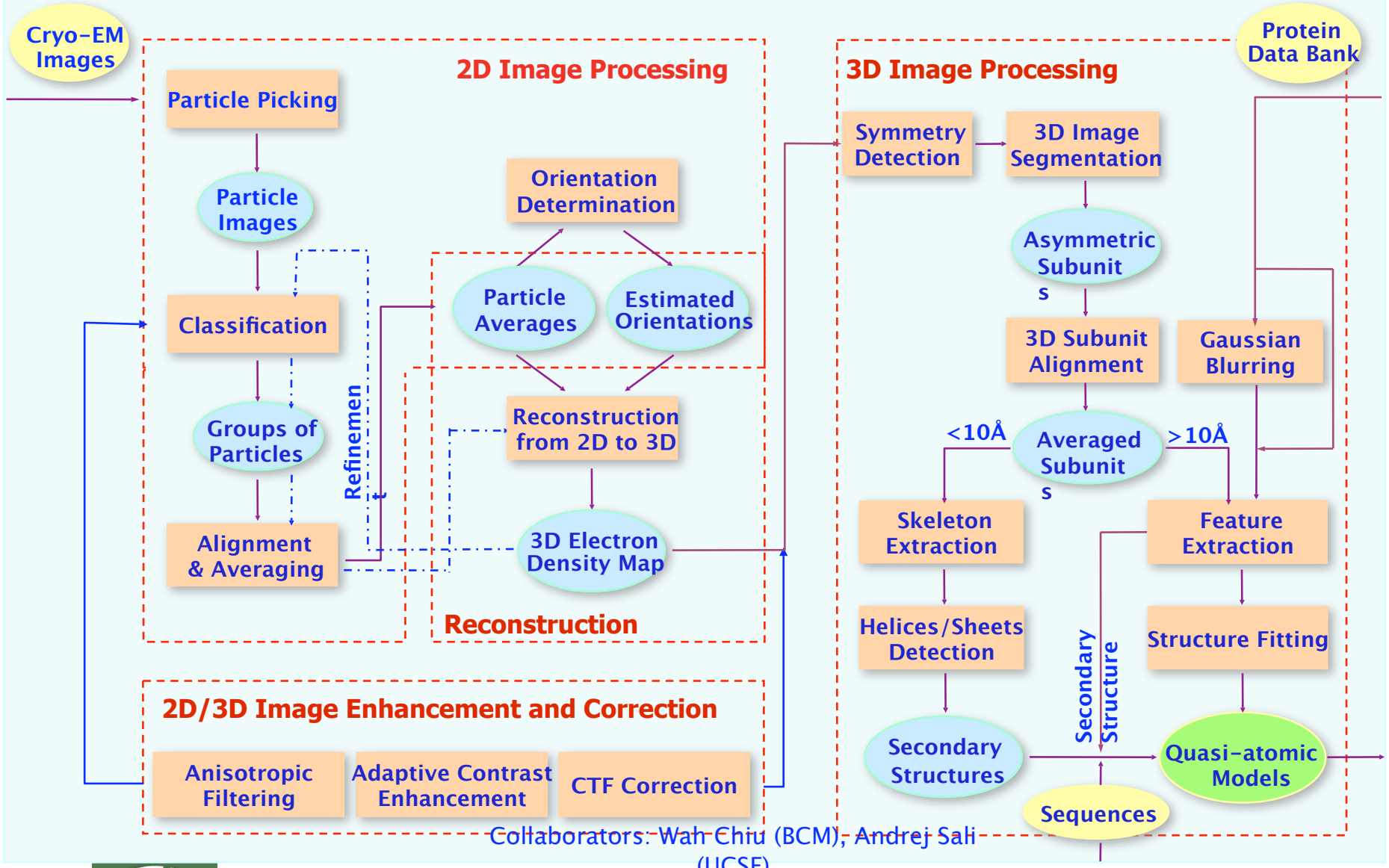
# Sinale Particle Cryo-EM: Pipeline




Collaborators: Wah Chiu (BCM), Andrej Sali (UCSF)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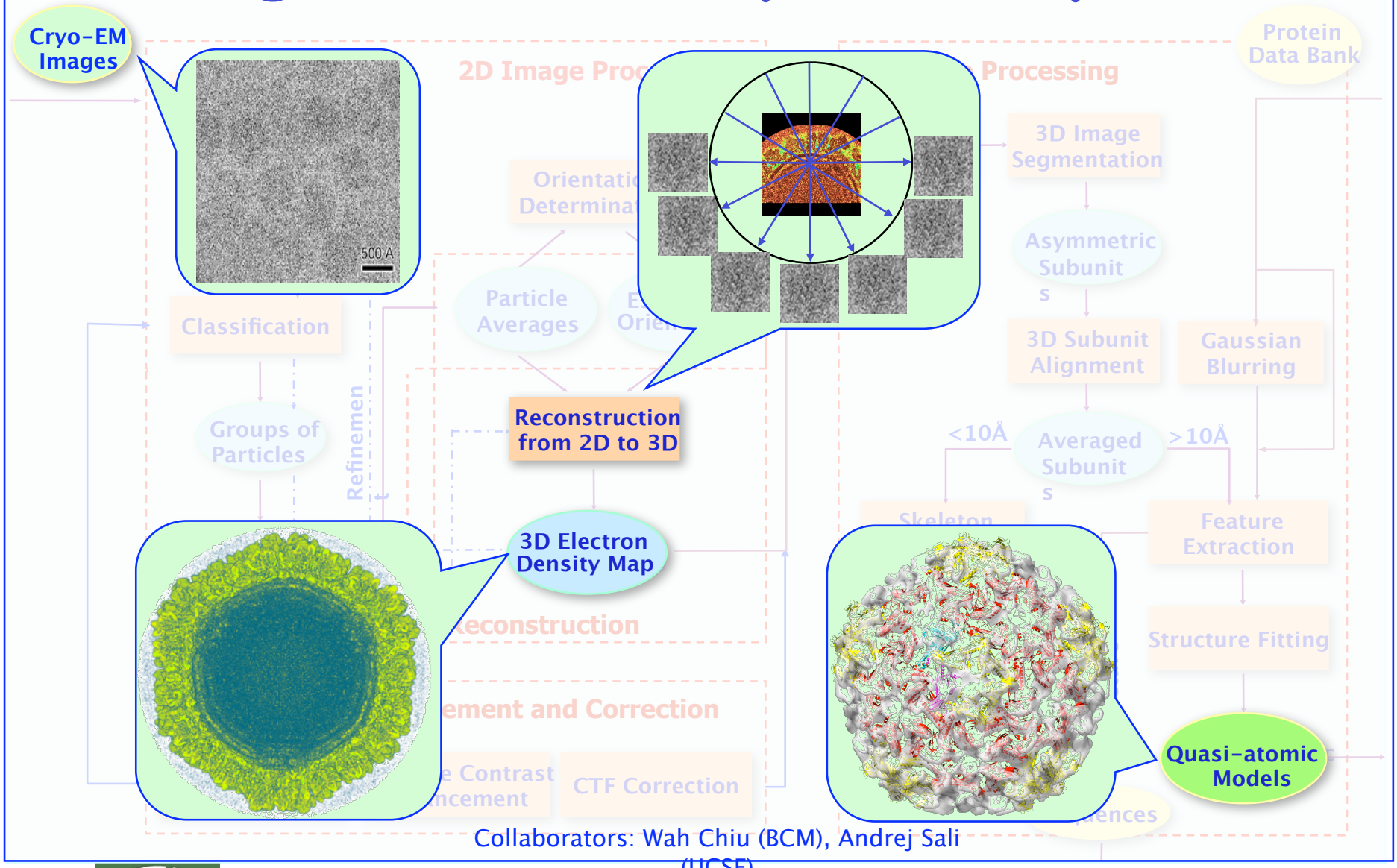
# Single Particle Cryo-EM Pipeline




Collaborators: Wah Chiu (BCM), Andrej Sali (UCSF)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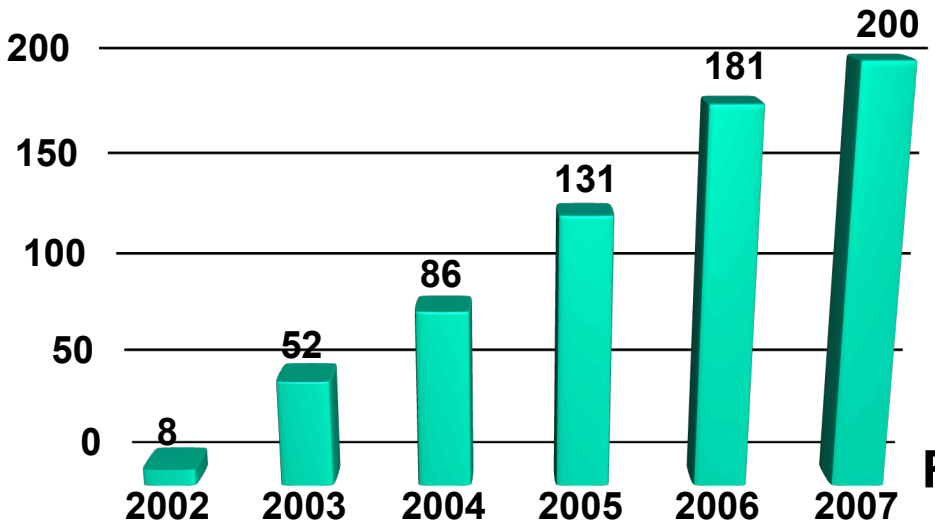
# 3D-Electron Microscopy DataBase

### 3D-EM Maps Deposited in EMDB

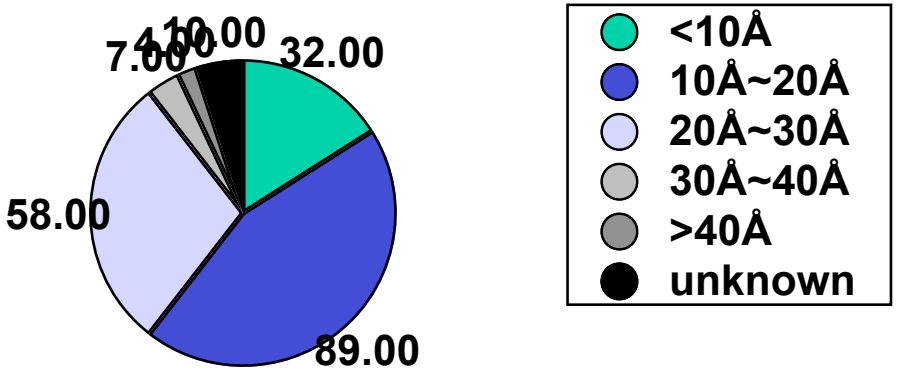



Data from: http://www.ebi.ac.uk/msd-srv/emsearch/, as of March 14th, 2006

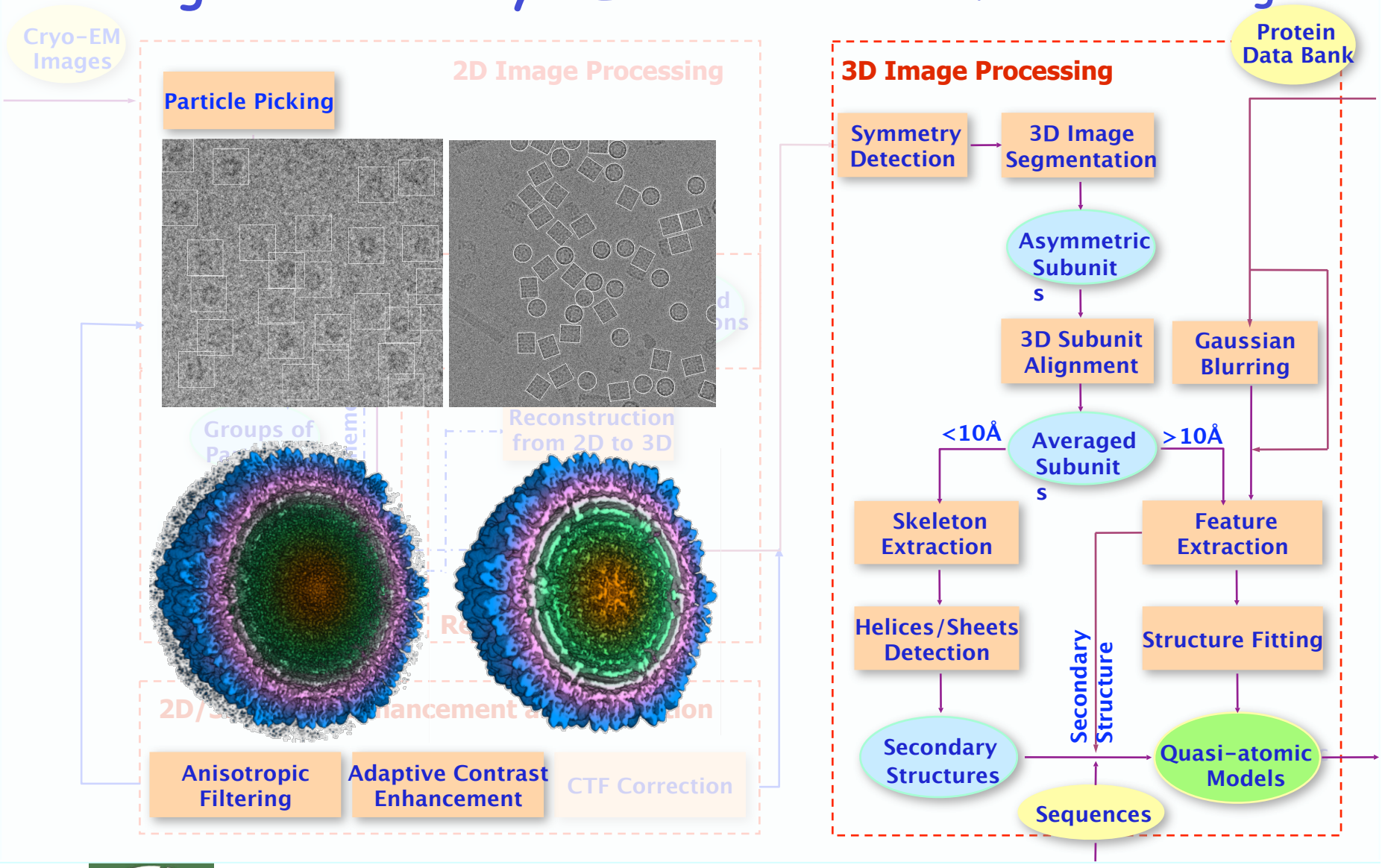
Automatic interpretation?

Quantitative analysis?

### Resolution Distribution



# Single Particle Cryo-EM: Towards Automatic Processing





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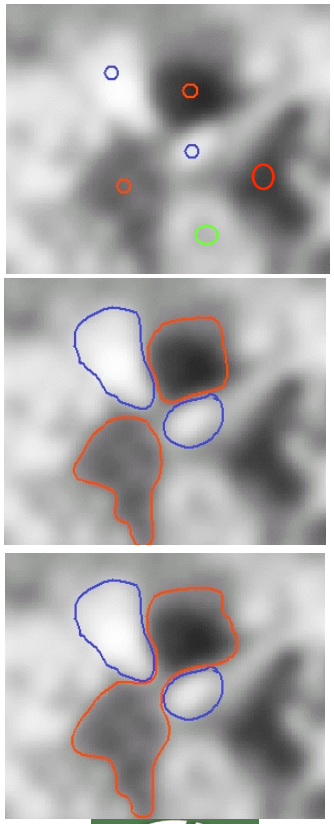
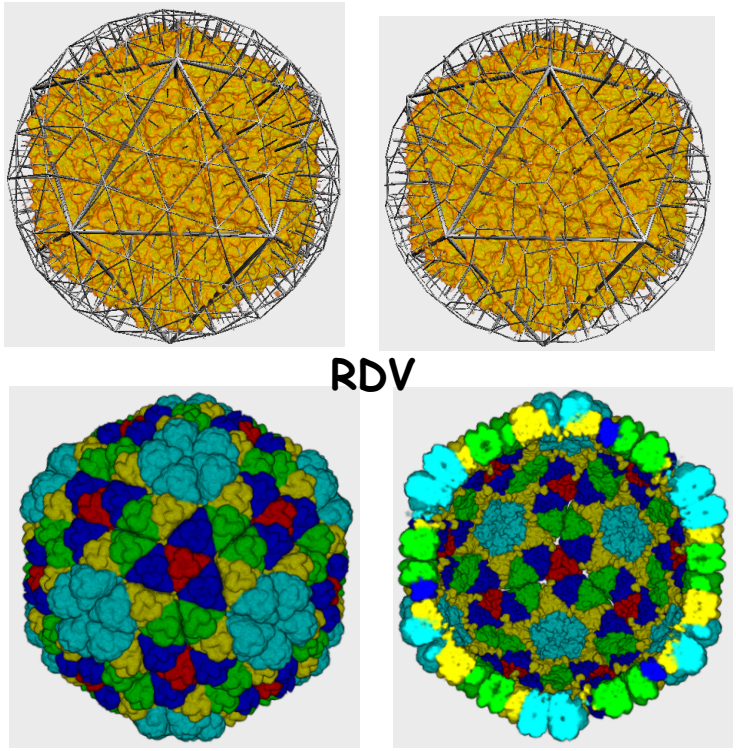
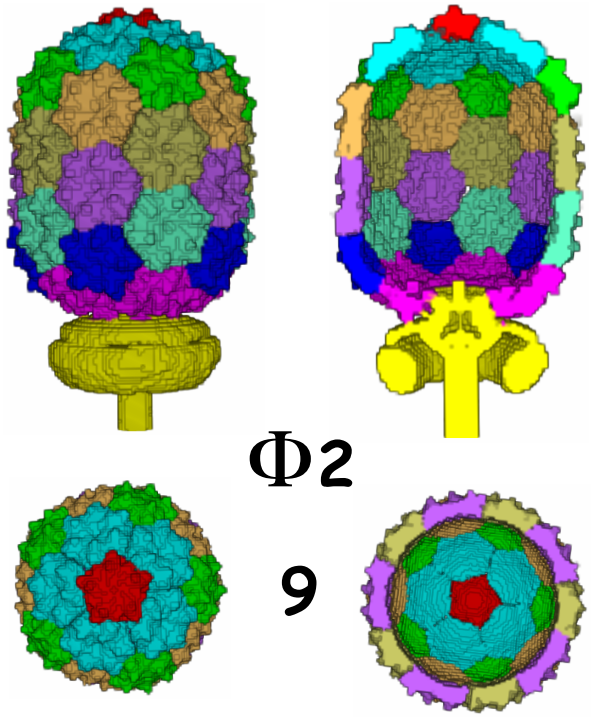
# Structure Elucidation 1(B): Boundary Segmentation

- Multi-seed Fast Marching Method
  - Classify the critical points based on local symmetry.
  - Each seed initializes one contour, with its group's membership.
  - Contours march simultaneously. Contours with same membership are merged, while contours with different membership stop each other.

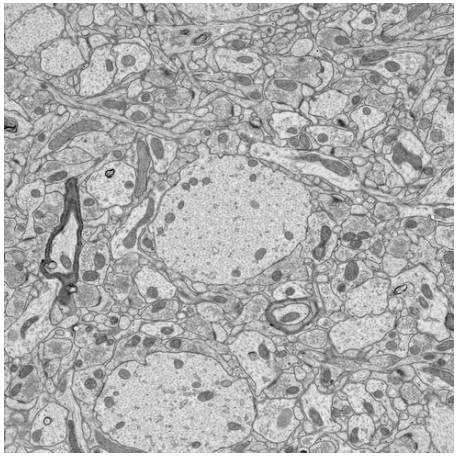


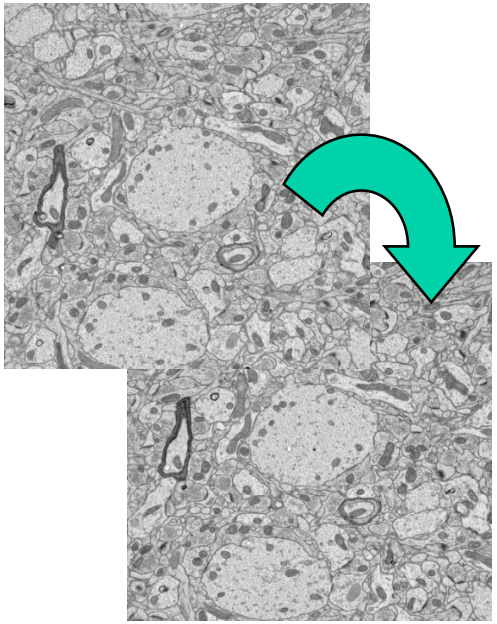


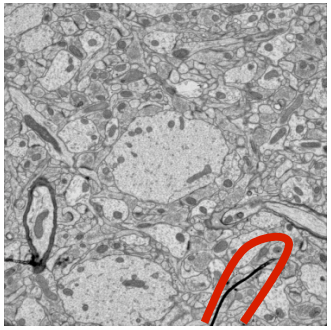



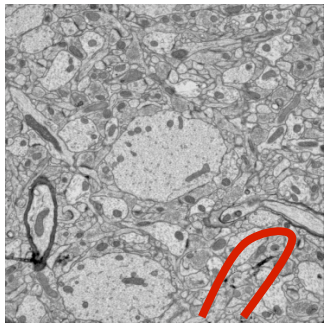

Z. Yu, and C. Bajaj, IEEE Trans.on Image Process, 2005. 144(1-2), pp. 132-143.

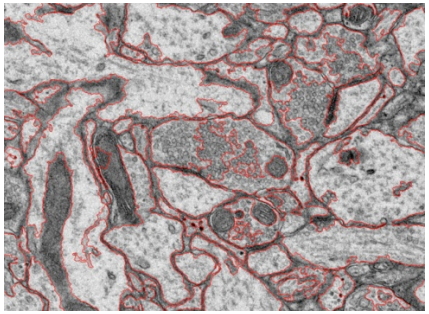
# Quantitative Morphology of Hippocampal Neurons

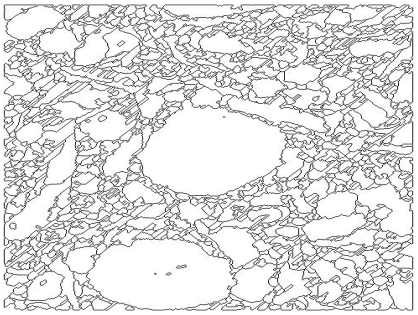






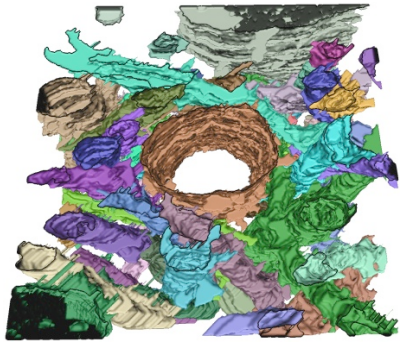


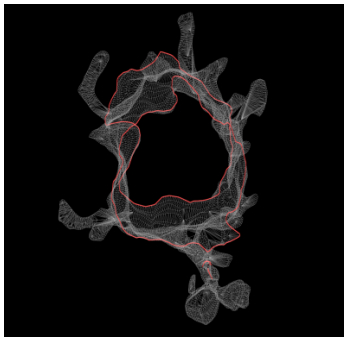


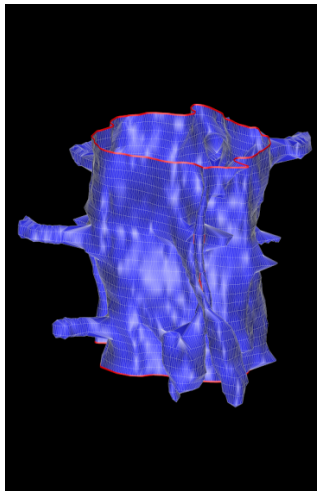


Transmission Electron Microscopy, Thin Sections:

Kristen Harris, University of Texas at Austin







Addtl. Collab: Tom Bartol, Salk Institute

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# Models2Analytics

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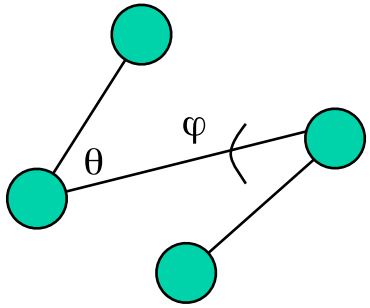
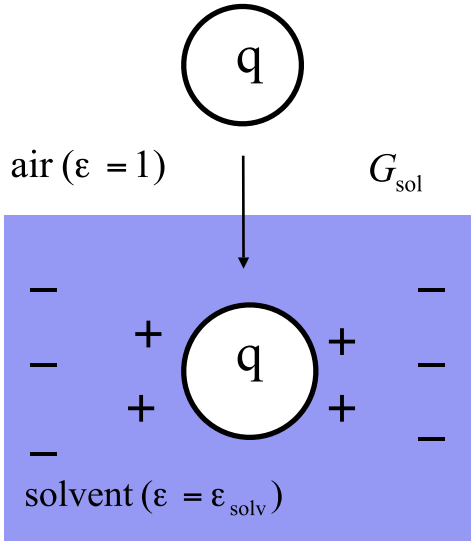
# Free Energy of a Macromolecule in Solvent

Total free energy : $G = E_{MM} + G_{sol} - TS$

$$E = E_b + E_\theta + E_\varphi + E_{vdw} + E_{elec}$$

$$G_{sol} = G_{cav} + G_{vdw} + G_{pol}$$




# How to Compute $G_{\text{pol}}$ ?

$$G_{\text{pol}} = \frac{1}{2}\int [\phi_{\text{solvent}}(\mathbf{r}) - \phi_{\text{air}}(\mathbf{r})]\rho(\mathbf{r})\,dV$$

- Poisson-Boltzmann (PB) Theory

$$-\nabla\cdot[\varepsilon(\mathbf{r})\nabla\phi(\mathbf{r})] = 4\pi\rho(\mathbf{r}) + 4\pi\lambda(\mathbf{r})\sum_{j=1} c_j^{\infty} q_j \exp(-q_j\phi(\mathbf{r})/k_B T)$$

finite difference, boundary element, finite element

| | |
|---|---|
| $\varepsilon$ | dielectric constant |
| $\phi$ | electrostatic potential |
| $\rho$ | solute charge density |
| $\lambda$ | ion accessibility parameter |
| $c_j^{\infty}$ | ion bulk concentration |
| $q_j$ | ion charge |
| $k_B$ | Boltzmann's constant |
| $T$ | temperature |

- Generalized Born (GB) Theory
  - Born formula (Born 1920), Generalized Born formula (Still 1990)

$$G_{\text{pol}} = -\frac{\tau}{2}\sum_{ij}\frac{q_i q_j}{[r_{ij}^2 + R_i R_j \exp(-\frac{r_{ij}^2}{4R_i R_j})]^{\frac{1}{2}}} \qquad R_i^{-1} = \frac{1}{4\pi}\int_{\text{ex}}\frac{1}{|\mathbf{r}-\mathbf{x}_i|^4}\,dV$$

$\tau = 1 - \frac{1}{\varepsilon_{\text{solv}}}$ $r_{ij}$ : distance between atom i and j

$q_i$ : charge of atom i $R_i$ : effective Born radius of atom i

**ex**: exterior to molecule

# How to Compute $G_{\text{pol}}$ ?

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finite difference, boundary element, finite element

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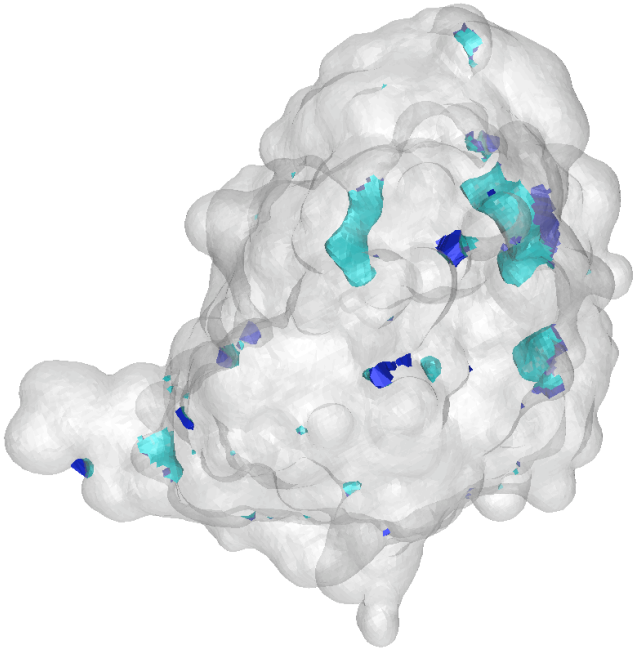
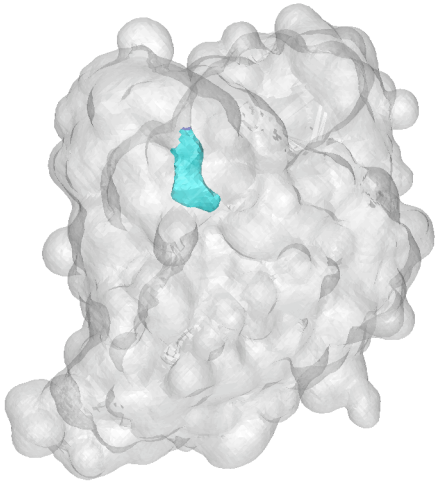
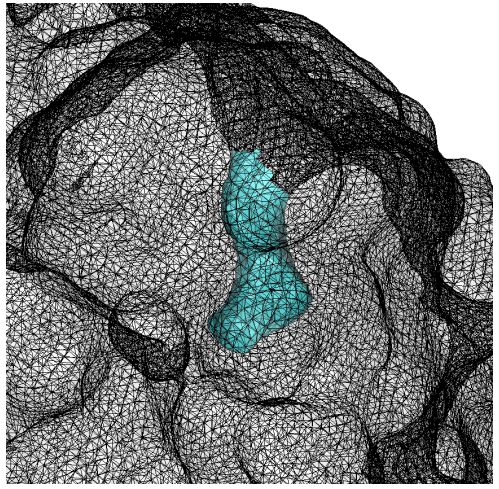
- Generalized Born (GB) Theory
  - Born formula (Born 1920)
    generalized Born formula (Still 1990)
  - methods to compute the Born radii:
    - pairwise summation methods: fast but not easy for force calculation
    - analytic integration methods: slow but straight forward for force

# Topological Noise Removal

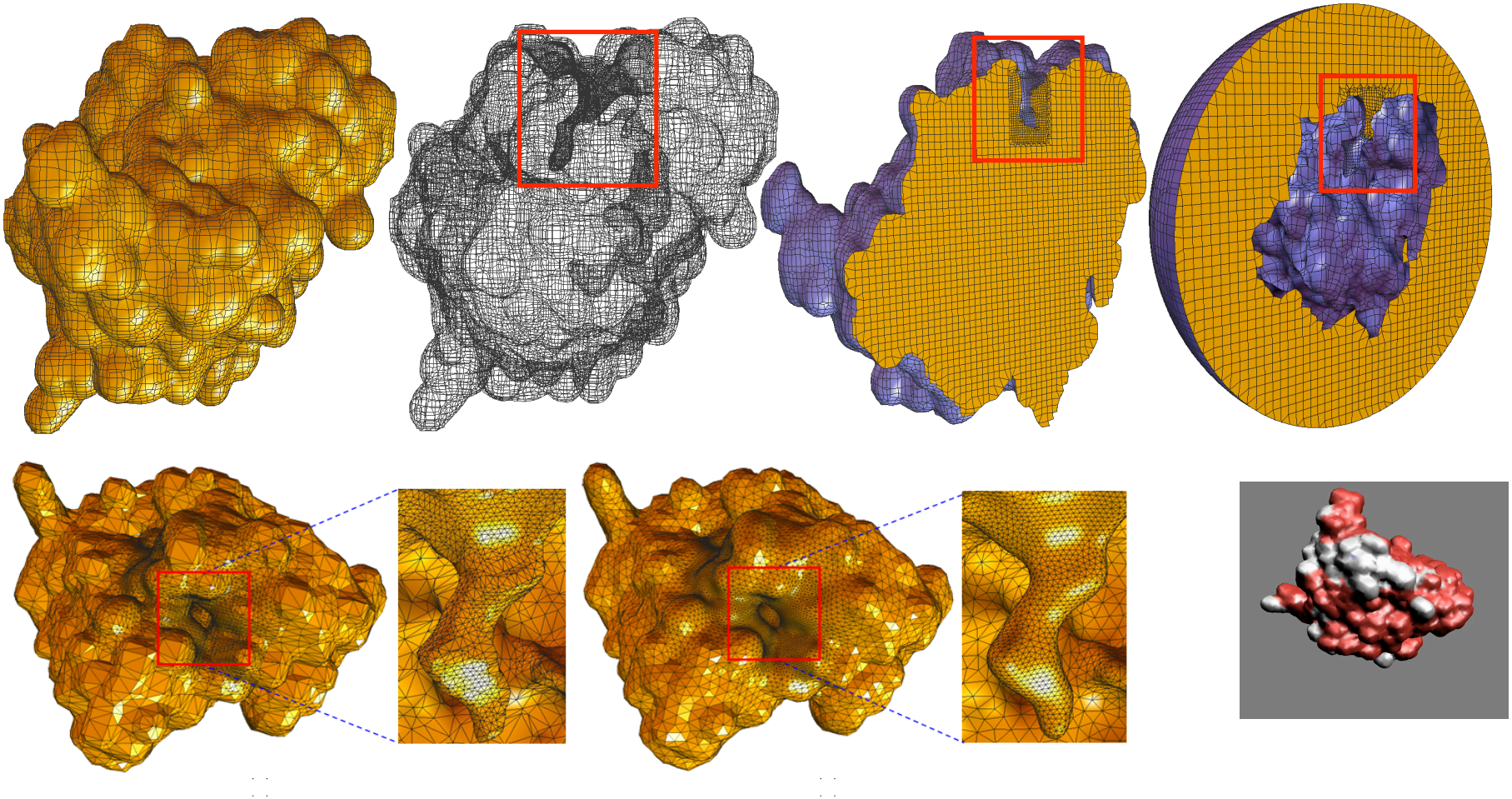






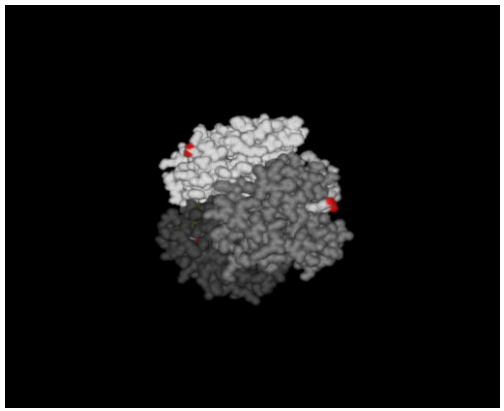
C.Bajaj, A. Gillette, S. Goswami, **Topology Based Selection and Curation of Level Sets** , TopoInVis 2007

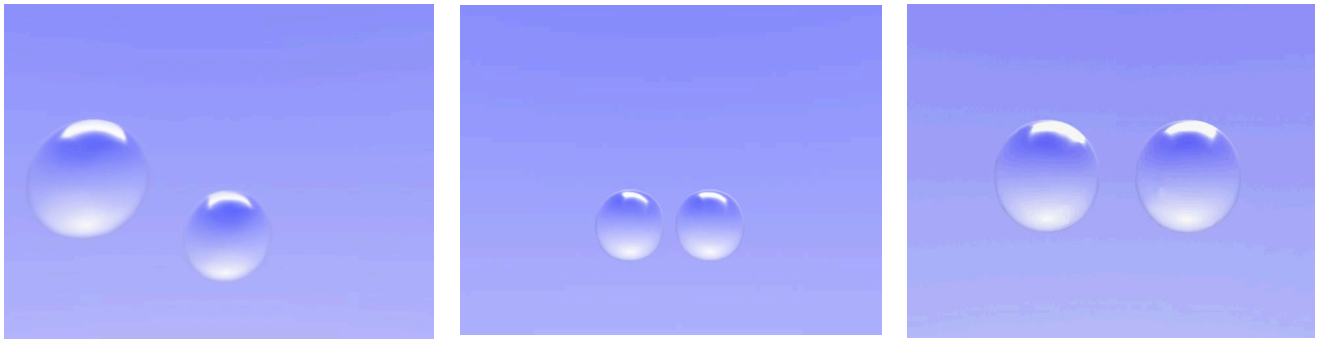
# Quality Boundary, Interior-Exterior Meshing



Y. Zhang, G. Xu, C. Bajaj
**Quality Meshing of Implicit Solvation Models of Biomolecular Structures**,
*Computer Aided Geometric Design (CAGD) , 23, 6, 2006, 510-530*

# Fast Dynamic BEM Electrostatics of Molecular and Cell Membrane Models





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# How to Compute $G_{pol}$ ?

$$G_{pol} = \frac{1}{2}\int [\phi_{solvent}(\mathbf{r}) - \phi_{air}(\mathbf{r})]\rho(\mathbf{r})\,dV$$

- Poisson-Boltzmann (PB) Theory

$$-\nabla\cdot[\varepsilon(\mathbf{r})\nabla\phi(\mathbf{r})] = 4\pi\rho(\mathbf{r}) + 4\pi\lambda(\mathbf{r})\sum_{j=1} c_j^{\infty} q_j \exp(-q_j\phi(\mathbf{r})/k_B T)$$

finite difference, boundary element, finite element

| | |
|---|---|
| $\varepsilon$ | dielectric constant |
| $\phi$ | electrostatic potential |
| $\rho$ | solute charge density |
| $\lambda$ | ion accessibility parameter |
| $c_j^{\infty}$ | ion bulk concentration |
| $q_j$ | ion charge |
| $k_B$ | Boltzmann's constant |
| $T$ | temperature |

- Generalized Born (GB) Theory
  - Born formula (Born 1920), Generalized Born formula (Still 1990)

$$G_{pol} = -\frac{\tau}{2}\sum_{ij}\frac{q_i q_j}{[r_{ij}^2 + R_i R_j \exp(-\frac{r_{ij}^2}{4R_i R_j})]^{\frac{1}{2}}} \qquad R_i^{-1} = \frac{1}{4\pi}\int_{ex}\frac{1}{|\mathbf{r}-\mathbf{x}_i|^4}\,dV$$

$\tau = 1 - \frac{1}{\varepsilon_{solv}}$ $r_{ij}$ : distance between atom i and j

**ex**: exterior to molecule

$q_i$ : charge of atom i $R_i$ : effective Born radius of atom i

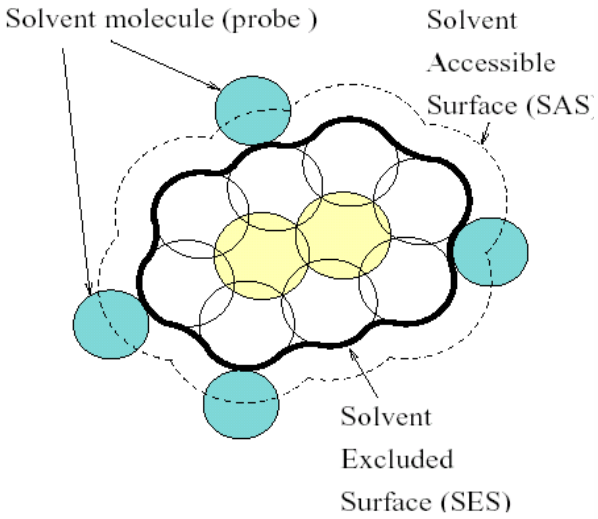
# Fast Computation of Born Radii

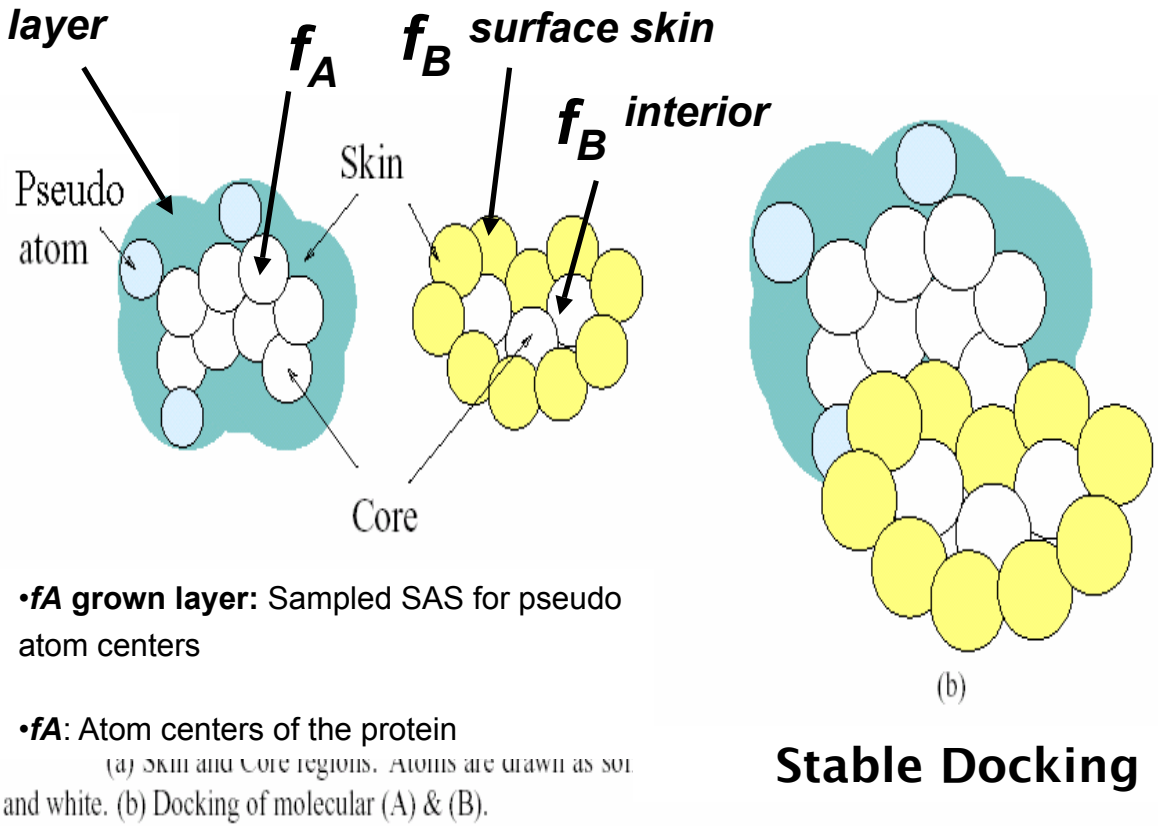
$$R_i^{-1} = \frac{1}{4\pi}\int_\Gamma \frac{(\mathbf{r}-\mathbf{x}_i)\cdot\mathbf{n}(\mathbf{r})}{|\mathbf{r}-\mathbf{x}_i|^4}\,dS \approx \frac{1}{4\pi}\sum_{k=1}^{N} w_k \frac{(\mathbf{r}_k-\mathbf{x}_i)\cdot\mathbf{n}(\mathbf{r}_k)}{|\mathbf{r}_k-\mathbf{x}_i|^4}, \qquad \mathbf{r}_k \in \Gamma$$

Algorithm:

1. Generate a model for the molecular surface $\Gamma$ .
2. Cubature: choose $w_k$ and $\mathbf{r}_k$ for higher order accuracy to be obtained for small $N$.
3. Fast Fourier summation to evaluate $R_i$ , $i = 1,\ldots,M$ .

# F^3 Dock: Fast Flexible Fourier Docking




(a) Skin and Core regions. Atoms are drawn as soi
and white. (b) Docking of molecular (A) & (B).

**Stable Docking**

- ***fA* grown layer:** Sampled SAS for pseudo atom centers
- ***fA***: Atom centers of the protein
- ***fB surface skin***: Surface atoms
- ***fB* interior atoms**:Atoms of B which are not surface atoms

Collaborators: Art Olson, Michel Sanner (TSRI)

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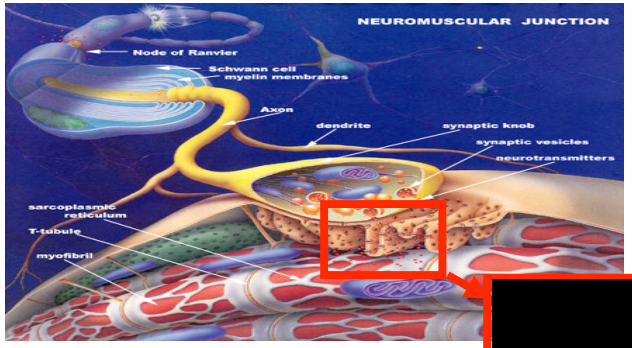
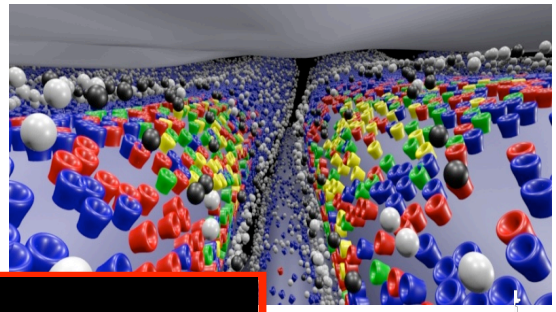
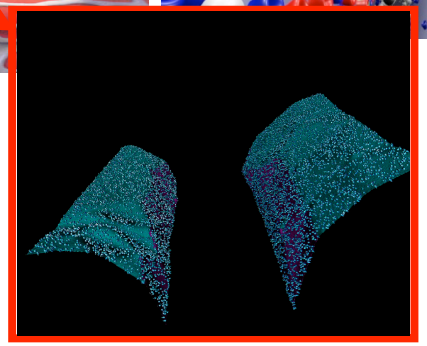
# Multiscale Modeling of the Neuro-Muscular Junction

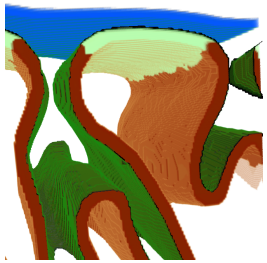


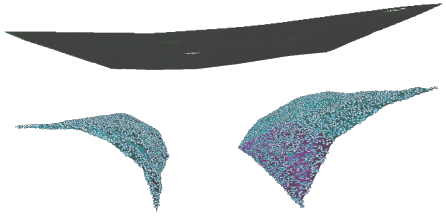





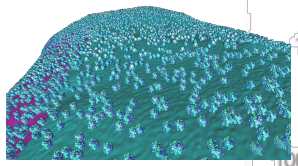
http://fig.cox.miami.edu/~cmallery/150/neuro/neuromuscular-sml.jpg http://mcell.salk.edu/

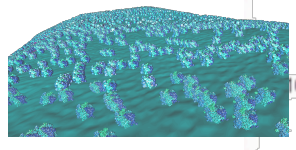
Multi-scale LOD

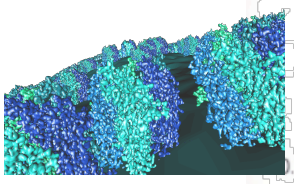


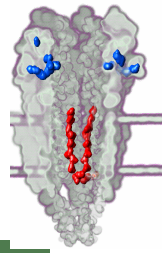


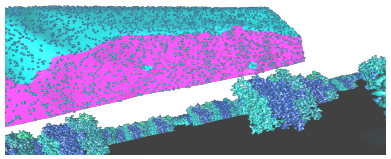


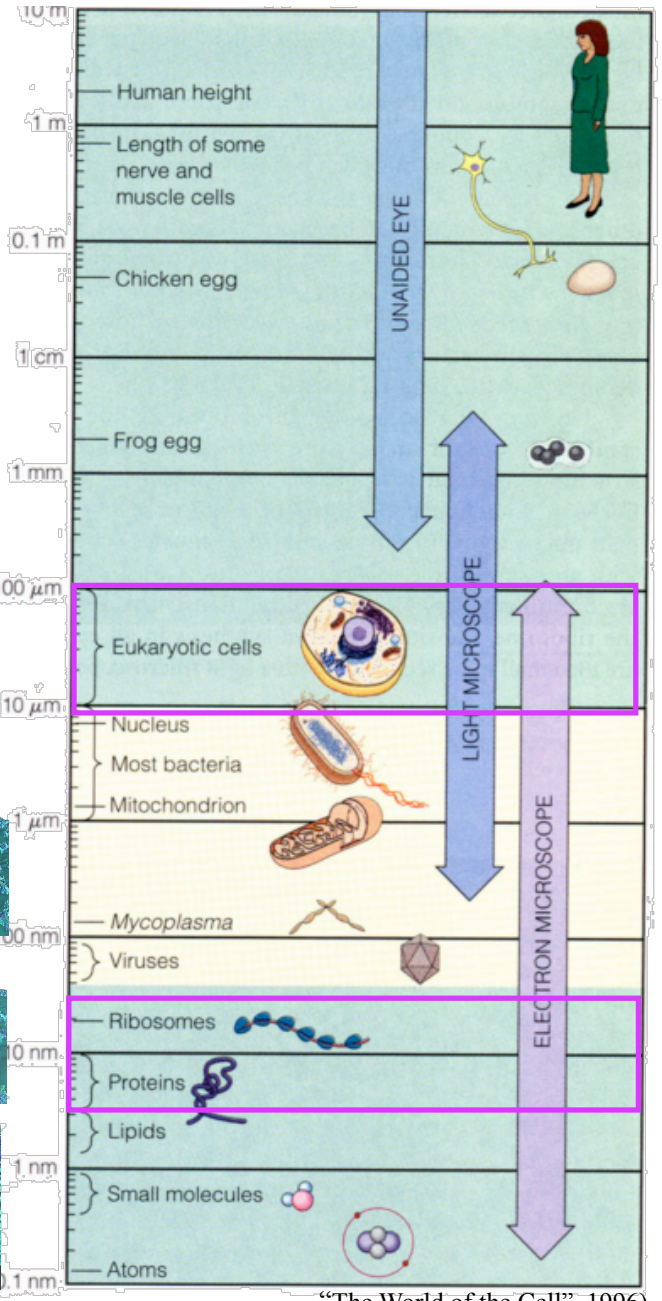













"The World of the Cell", 1996)

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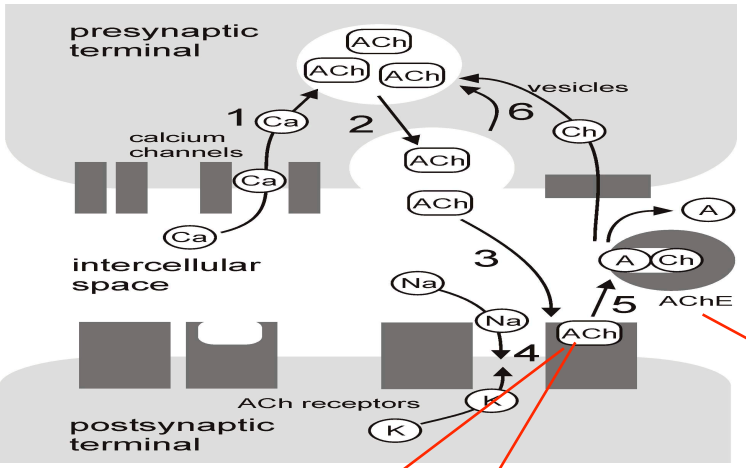
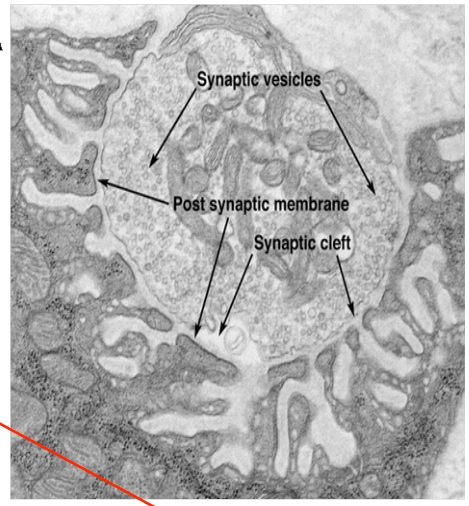
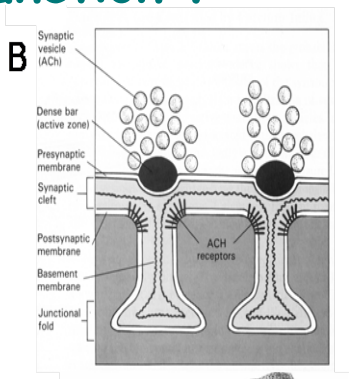
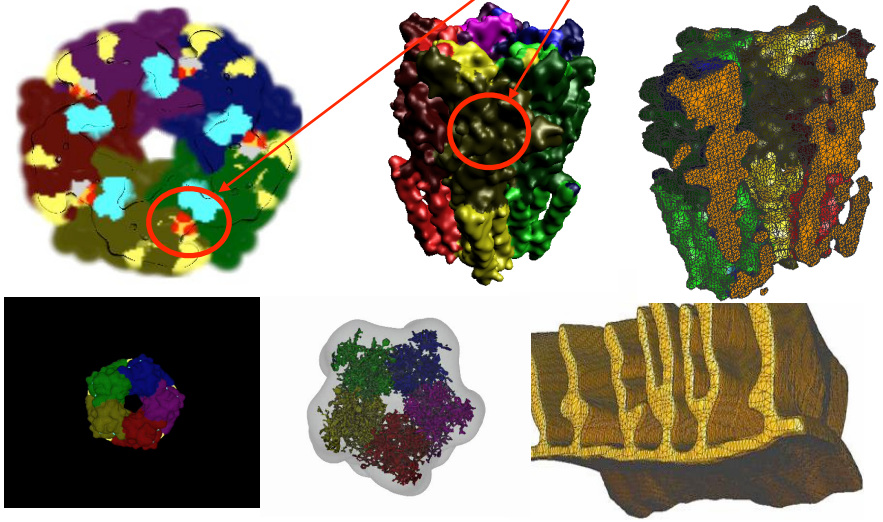
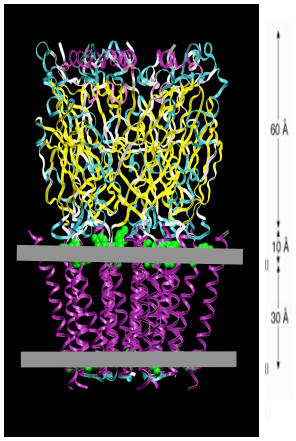
# How do Synapses Occur at the Neuro-Muscular Junction ?

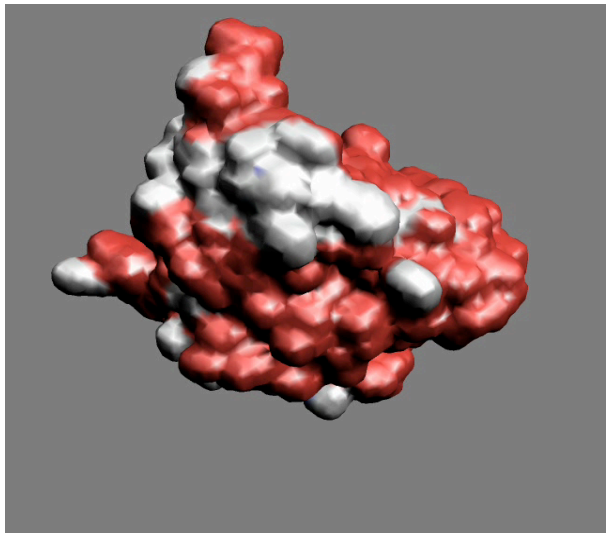





•Y. Zhang, C. Bajaj, B. Sohn, *Special issue of Computer Methods in Applied Mechanics and Engineering (CMAME) on Unstructured Mesh Generation, 2004.*

•Y. Song, Y. Zhang, T. Shen, C. Bajaj, J. A. McCammon and N. A. Baker, *Finite Element Solution of the Steady-State Smoluchowski Equation*, *Biophysical Journal, 86(4):2017-2029, 2004.*



Collaborators: Nathan Baker (Wash. U), Andy McCammon, Mike Holst, Mark Ellisman (UCSD)

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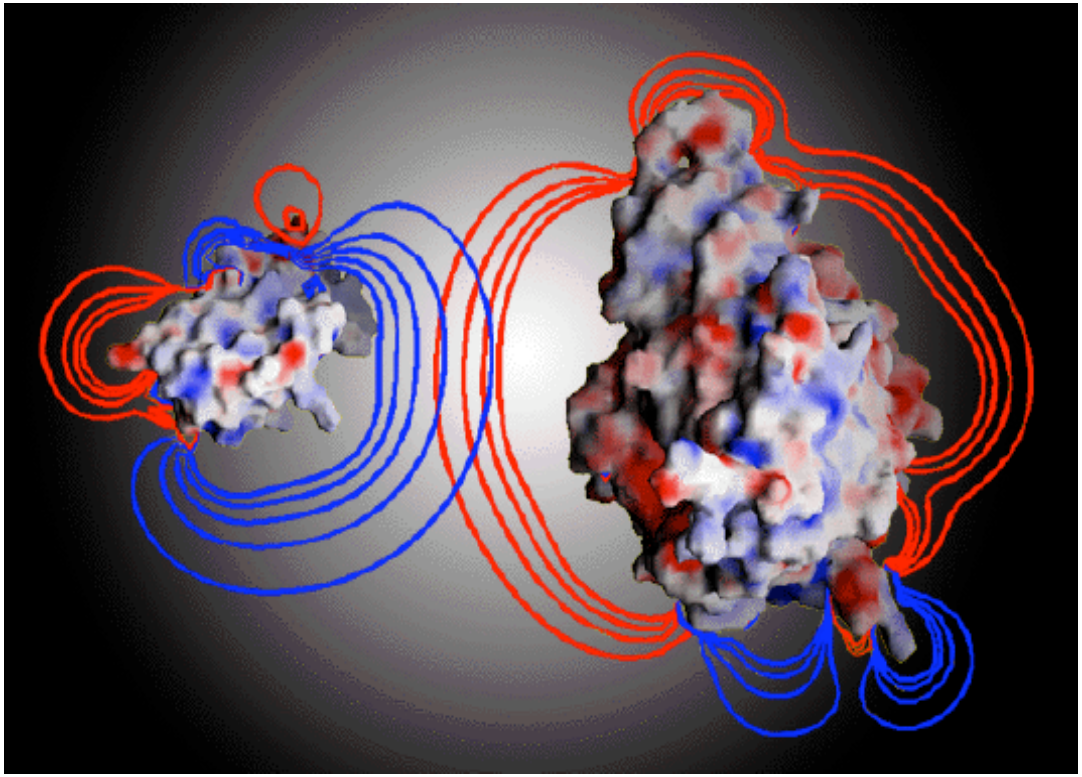
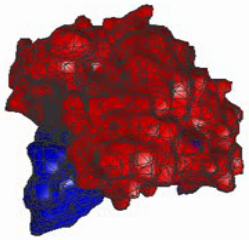
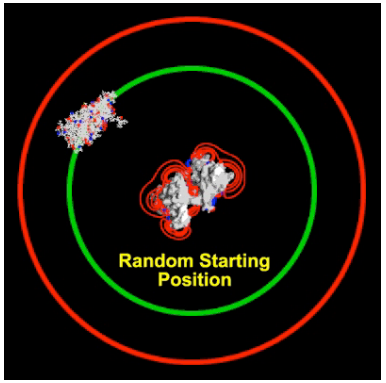
# Fas2 meets AChE



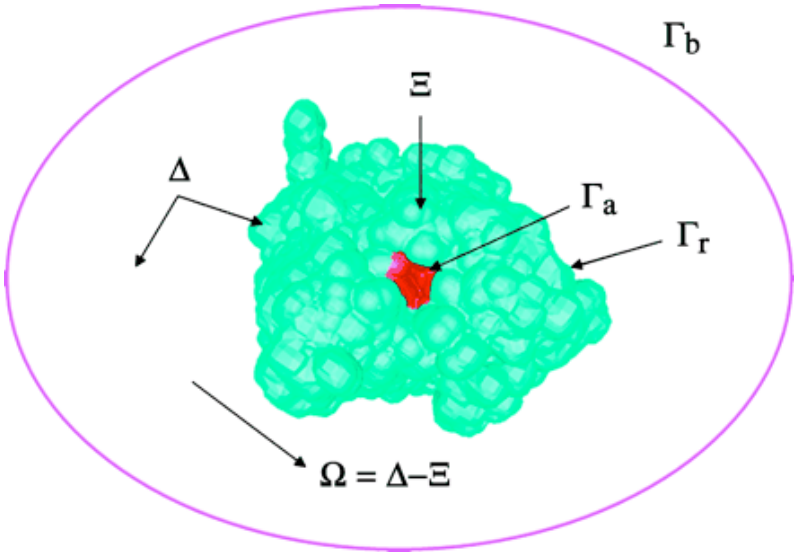




# Steady State Smulochowski Equation

## (Diffusion of multiple particles in a potential field)

$$\vec{J}p(\vec{r}) = D(\vec{r})[\nabla p(\vec{r}) + \beta p(\vec{r})\nabla U(\vec{r})]$$




- Δ -- entire domain
- Ξ -- biomolecular domain
- Ω -- free space in Δ
- $\Gamma_a$ – reactive region
- $\Gamma_r$ – reflective region
- $\Gamma_b$ – boundary for Δ

$$p(\vec{r}) = p_{bulk} \text{ for } \vec{r} \in \Gamma_b$$

$$p(\vec{r}) = 0 \text{ (Dirichlet BC) for } \vec{r} \in \Gamma_a$$

$$\text{or } \vec{n} \times \vec{J}p(\vec{r}) = \alpha(\vec{r})\, p(\vec{r}) \text{ (Robin BC)}$$

$$\vec{n} \times \vec{J}p(\vec{r}) = 0 \text{ for } x \in \Gamma_r$$

Diffusion-influenced biomolecular reaction rate constant :

$$k = \frac{\int_{\Gamma_a} \vec{n} \times \vec{J}p(\vec{r})\, dS}{p_{bulk}}$$

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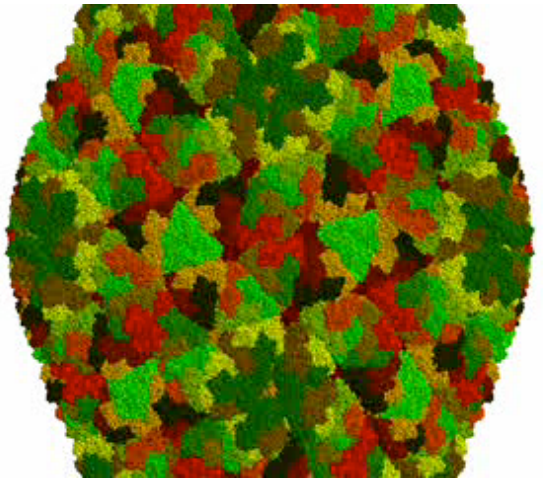
# Interrogative Scalable Visualization

- **Novel techniques**
  - Surface/2D Textures/3D Texture based rendering exploit hardware acceleration
  - Multi-dim Transfer Functions for Regions of Interest
  - Compressed data processing
  - Parallelism (back-end PC cluster)
  - Hierarchical processing and rendering



**TexMol**


C.Bajaj, I. Ihm, S. Park, *ACM Trans. on Graphics*, 20, 1, 10-28, 2001

C Bajaj, P Djeu, V Siddavanahalli, A Thane, *IEEE visualization*, 2003. 243-250.

C. Bajaj, J. Castrillon-Candas, S. Vinay, A. Xu, *Structure*,13,3,2005,463-471

X. Zhang, C. Bajaj, *IEEE Symp. On Parallel, Large Data Visualization*, 2001, 51-58
X. Zhang, C. Bajaj *Eurographics-IEEE TVCG Symposium on Visualization 2002, 9-18*



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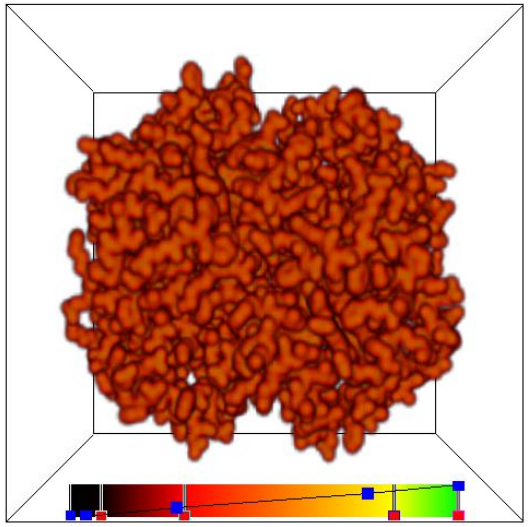
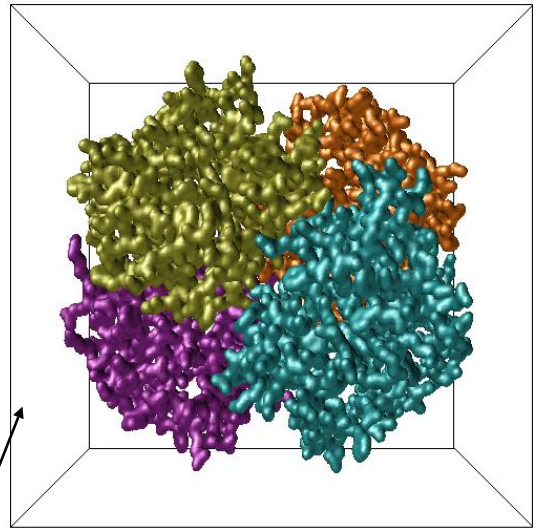
GroEL Data courtesy: Dr. Wah Chiu

# Topological Analysis & Visualization

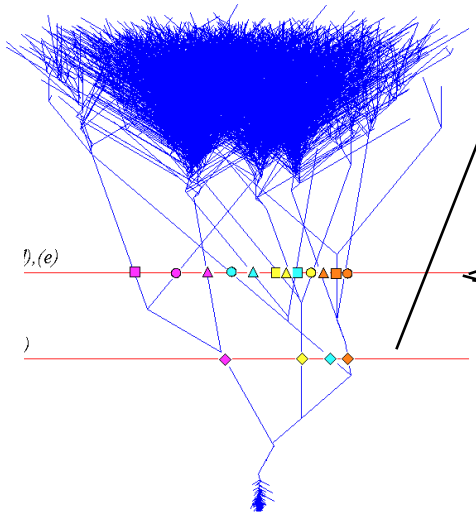


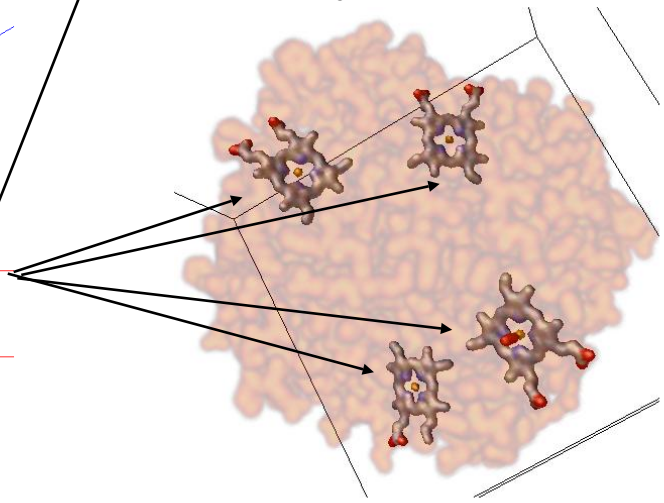


Four Polypeptide chains

Contour Tree
of
Electron Density Map

3D chemical bonding
structures
with different levels





Functional groups

Atoms belonging to the same contour have stronger linkage

Each chain consists of heme, iron, and globin


•M. van Kreveld, R. van Oostrum, C. Bajaj, V. Pascucci, and D. Schikore, *Chap5, pg 71 - 86, 2004 ed. by S. Rana, John Wiley & Sons, Ltd, 2004*

•C. Bajaj, V.Pascucci, and D.Schikore, *Proceedings of the 1997 IEEE Visualization Conference,167-173, October 1997 Phoeniz, Arizona*



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# Today's Examples

- Ss TEM, Cryo-EM and Tomographic Imaging to Ultra-Structure to Geometry (Volumetric Image Processing)
- Geometry to Finite Element Meshes (Geometric Modeling)
- Faster Solvers (Geometry Adaptive Integral / Differential Equations Solving)
- Quantitative Analysis of Structure & Properties - Topological, Combinatorial, Metric (Computational Geometry)
- Immersive/Exploratory (Computer Graphics, Visualization)

# What could you learn from this course ?

- Techniques and tools to generate computer structure (geometry) models of life forms with spatial realism
- Techniques and tools to computationally model and simulate physiological function
- Techniques and tools to analyze, interrogate & visualize structure and function

# Additional Reading for the Next Few Lectures

- C.Bajaj "Multivariate Polynomial/Shape Representations"
  http://www.cs.utexas.edu/~bajaj/cs384R08/reading/Multivar-Polynomial_representation.pdf
  http://www.cs.utexas.edu/~bajaj/cs384R08/reading/Multivar-BBezier-tutorial.pdf
  http://www.cs.utexas.edu/~bajaj/cs384R08/reading/Repofsolids.pdf
- C. Bajaj "Modeling and Visualizing Virus Ultrastructure"

http://www.cs.utexas.edu/~bajaj/cs384R08/reading/b05-virus-arch.pdf

- C. Bajaj and Z. Yu "Geometric Processing of 3D Cryo-EM"

http://www.cs.utexas.edu/~bajaj/cs384R08/reading/by05-hndbk.pdf